

AMENDMENTS TO THE CLAIMS

Claim 1 (currently amended). A modified hirudin molecule being substantially non-immunogenic or less immunogenic than non-modified wild-type hirudin ~~having essentially the same biological specificity and activity when used in vivo, comprising amino acid residues substitutions compared with the non-modified parental molecule, which cause a reduction or an elimination of one or more of T-cell epitopes acting in the parental non-modified molecule as MHC class II binding ligands and stimulating T-cells, said modified hirudin molecule has the (M) and having the amino acid residue sequence of SEQ ID NO: 2:~~

V V Y T D C T E S G Q N X¹ C X² C E G S V X³ C G Q G N K C X⁴ X⁵ G S D G E K N Q C X⁶ T
G E G T P X⁷ X⁸ E S H N X⁹ G D X¹⁰ E E I P E E Y L Q

wherein;

X¹ = T or L

X² = T or A or H or Q or T or L;

X³ = A or G or H or K or N or P or Q or R or V;

X⁴ = A or D or E or G or H or K or N or Q or R or S or T or I;

X⁵ = A or D or E or G or H or K or N or P or Q or R or S or T or L;

X⁶ = A or T or V;

X⁷ = T or K;

X⁸ = A or T or P;

X⁹ = E or N or R or D;

X¹⁰ = H or F

and ~~whereby~~ wherein the wild-type sequence of hirudin (in which X¹ = L, X² = L, X³ = V, X⁴ = I, X⁵ = L, X⁶ = V, X⁷ = K, X⁸ = P, X⁹ = D and X¹⁰ = F) is excluded.

Claim 2 (currently amended). [[A]] The modified hirudin molecule according to of
claim 1, wherein

X1 = L,

X2 = L,

X3 = V,

X⁴ = A or D or E or G or H or K or N or Q or R or S or T or I;

$X^5 = A \text{ or } D \text{ or } E \text{ or } G \text{ or } H \text{ or } K \text{ or } N \text{ or } P \text{ or } Q \text{ or } R \text{ or } S \text{ or } T \text{ or } L$;

$X^6 = A \text{ or } T \text{ or } V$;

$X^7 = T \text{ or } K$;

$X^8 = A \text{ or } T \text{ or } P$;

$X^9 = E \text{ or } N \text{ or } R \text{ or } D$; and

$X^{10} = H \text{ or } F$.

Claim 3 (currently amended). ~~[[A]] The modified hirudin molecule according to of~~
claim 2, wherein

$X^6 = V$;

$X^7 = K$;

$X^8 = P$;

$X^9 = D$; and

$X^{10} = F$.

Claim 4 (currently amended). ~~[[A]] The modified hirudin molecule according to of~~
claim 3, wherein

~~[[X4]]~~ $X^4 = A \text{ or } R$, and

~~[[X5]]~~ $X^5 = A \text{ or } H$.

Claim 5 (currently amended). ~~[[A]] The modified hirudin molecule according to of~~
claim 4 ~~having the sequence M1 of Table A~~ wherein $X^4 = A$, and $X^5 = A$.

Claim 6 (currently amended). ~~[[A]] The modified hirudin molecule according to of~~
claim 4 ~~having the sequence M2 of Table A~~ wherein $X^4 = R$, and $X^5 = H$.

Claim 7 (currently amended). A modified hirudin molecule ~~according to claim 1~~
having ~~[[a]]~~ an amino acid residue sequence selected ~~from~~ from the group consisting of ~~M1—M81~~
~~as specified in Table A~~ SEQ ID NO: 4 through SEQ ID NO: 84, inclusive.

Claim 8 (currently amended). A pharmaceutical composition comprising [[a]] the modified hirudin molecule of ~~any of the claims 1—7~~ claim 1, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 9 (currently amended). A peptide ~~molecule~~ having the amino acid residue sequence CILGSDGEKNQCVTGEGTPKPESHNDGDFE (A) (SEQ ID NO: 1) or a sequence ~~track~~ consisting of at least 9 consecutive amino acid residues of ~~any of said peptide molecules~~ SEQ ID NO: 1 having a potential MHC class II binding activity ~~and created from the primary sequence of non-modified hirudin, whereby~~ wherein said peptide ~~molecule or sequence track~~ has a stimulation index of > 1.8 in a biological assay of cellular proliferation and said index is taken as the value of cellular proliferation scored following stimulation by [[a]] the peptide and divided by the value of cellular proliferation scored in control cells not in receipt of the peptide.

Claim 10 (cancelled).

Claim 11 (new). A pharmaceutical composition comprising the modified hirudin molecule of claim 2, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 12 (new). A pharmaceutical composition comprising the modified hirudin molecule of claim 3, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 13 (new). A pharmaceutical composition comprising the modified hirudin molecule of claim 4, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 14 (new). A pharmaceutical composition comprising the modified hirudin molecule of claim 5, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 15 (new). A pharmaceutical composition comprising the modified hirudin molecule of claim 6, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 16 (new). A pharmaceutical composition comprising the modified hirudin molecule of claim 7, optionally together with a pharmaceutically acceptable carrier, diluent or excipient.